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EXAMINER	
SLOBODYANSKY, ELIZABETH	

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/993,874	Applicant(s) VIVIANI ET AL.	
	Examiner Elizabeth Slobodyansky, PhD	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 6-11* is/are pending in the application.

4a) Of the above claim(s) *3 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-8,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7, 12*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed February 17, 2004 amending the specification to correct a typographical error and delete an embedded hyperlink, amending claims 1 and 3, deleting claims 2, 4 and 5 and adding claims 6-11 has been entered.

The Declaration under 37 CFR 1.132 by Drs. Vadim Viviani and Yoshihiro Ohmiya filed February 17, 2004 has been entered.

Claims 1, 3 and 6-11 are pending.

Election/Restrictions

Amended claim 3 and newly submitted claim 9 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Invention of claims 1, 6-8, 10 and 11 and invention of claims 3, 9 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, represent structurally different polynucleotides encoding structurally and functionally different luciferases. Therefore, where structural identity is required, such as for hybridization or expression, the different sequences have different effects.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 3 and 9 are withdrawn from

consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1, 6-8, 10 and 11 are under consideration.

Priority

Applicant's intent to submit a certified copy of the Italian application when it becomes available is noted (Remarks of February 17, 2004, page 5).

Information Disclosure Statement

The reference "AR" to Roda et al. on the information disclosure statement filed November 14, 2001 has been lined through because Roda et al. are Editors of "Proceedings of the 10th International Symposium on Bioluminescence and Chemiluminescence held at Bologna, Italy, September 1998". Applicants submitted only the Title page of said Proceedings in parent application 09/516,958. However, the abstract by Viviani et al. that is part of said Proceedings has been submitted in 09/516,958 and has been considered.

Specification

The specification is objected to because the description of Figures 1A-1C on page 4, lines 4-6, indicates SEQ ID NO:1. However, the nucleotide sequence shown at the Figures appears to be different from SEQ ID NO:1 in at least the following: "A" is absent at the figure at position corresponding to position 1090 of SEQ ID NO:1.

Appropriate correction is required.

Claim Objections

Claims 6-8, 10 and 11 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 6 depends from claim 1. Claim 1 recites highly stringent conditions under which the nucleic acid molecules that are at least more than 95% identical to SEQ ID NO:1 will hybridize. However, claim 6 recites "at least 90% identity". Claims 7, 8, 10 and 11 depend from claim 6.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to recite "a maximum λ of approximately 549 nm". While there is support in the specification for "a maximum λ = 549 nm" (page 4, line 23, for example), the examiner is unable to locate adequate support in the specification for the word "approximately" in said phrase. Thus there is no indication that luciferase

emitting at "a maximum λ of approximately 549 nm" was within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 6-8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding SEQ ID NO:2, including SEQ ID NO:1, and a DNA that hybridizes to SEQ ID NO:1 under high stringency conditions comprising a wash in 0.1 x SSC/0.1% SDS for 15 min at 68°C and encodes a luciferase emitting at λ_{max} 549 nm, does not reasonably provide enablement for a DNA that is 90% identical to SEQ ID NO:1 and encodes a luciferase emitting at λ_{max} 549 nm. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 6, with dependent claims 7, 8, 10 and 11, is so broad as to encompass DNAs having 90% identity to SEQ ID NO: 1 and encoding a luciferase emitting at λ_{max} 549 nm. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutant luciferase enzymes and genes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and amino acid sequence of single *Prixothrix vivianii* luciferase (SEQ ID NO:1 and SEQ ID NO: 2, respectively).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any nucleic acid molecule having 90% identity to SEQ ID NO: 1 encoding a luciferase emitting at λ_{max} 549 nm because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting luciferase activity; (B) the general tolerance of luciferase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any luciferase residues with an expectation of obtaining the requisite luciferase function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any nucleic acid molecule with 90% identity to SEQ ID NO:1 encoding a luciferase emitting at λ_{max} 549 nm. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of luciferases and genes therefor having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-8, 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, with dependent claims 6-8, 10 and 11, recites "a maximum λ of approximately 549 nm". The metes and bounds of the term "approximately" are not defined in the specification and can mean different ranges in the art rendering the claim unclear.

Claim 6, with dependent claims 7, 8, 10 and 11, is unclear as reciting "at least 90% identity" without indicating to which sequence the claimed sequence is identical. Amending the claim to recite "at least 90% identity to SEQ ID NO:1" would obviate this rejection.

Claim 11 recites the limitation "the vector as defined in Claim 8". There is insufficient antecedent basis for this limitation in the claim because claim 8 is drawn to a recombinant host cell not a vector.

Response to Amendment

The Declaration under 37 CFR 1.132 by Drs. Vadim Viviani and Yoshihiro Ohmiya filed February 17, 2004 is sufficient to overcome the rejection of claims 1-5 based upon Viviani et al. The inventors stated that the 3rd author in "the Article, Etelvino J.H. Bechara was merely working under the direction of Vadim R. Viviani and/or Yoshihiro Ohmiya, who are the sole inventors of the present application" (Declaration, page 1).

Response to Arguments

Applicant's arguments filed February 17, 2004 have been fully considered.

With regard to Figures 1 and 2, the examiner confirms that said Figures are currently present in the specification. In view of the issues discussed above, the cancellation of these Figures will be approved. It should be made by the amendment containing also amendment to the current Figure 3 and its description.

With regard to the Sequence Listing, the examiner notes that the US PTO has made no changes to the Sequence Listing. Thus, the current Sequence Listing is the one present in the application at the time of filing. According to the US PTO databases, SEQ ID NOs: 1 and 2 in the Sequence Listing in the instant application are 100% identical to SEQ ID NOs: 1 and 2 in parent application 09/516,958.

The 112, 1st paragraph, written description and enablement, rejections of claim 1 are withdrawn in view of the amendment. However, claim 1 is currently rejected in view of the new matter introduced by the amendment. The 112, 1st paragraph, rejections of claims 2 and 4 are moot in view of the cancellation of these claims.

Amended claim 3 is withdrawn for the reasons discussed above. It is noted that claim 3 as filed was drawn to SEQ ID NO:1. The amended claim 3 is drawn to SEQ ID NO:3 without markings to indicate that the sequence has been changed relative to the immediate prior version of the claim. As indicated in the preceding Office action mailed December 13, 2002 (page 11), for the purpose of examination the examiner considered claim 1 as reciting SEQ ID NO:2 not SEQ ID NO:3.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

May 11, 2004